## ABOUT CPT-11 (CAMPTO<sup>TM</sup>)



## Differences between topoisomerase 1 metabolism among mice and men

Joël Sternheimer European University of Research, i rue Descartes 75005 Paris

Several human clinical studies are currently being carried on concerning a topoisomerase 1 inhibitor, CPT-11 or Campto, following "encouraging" preliminary trials on mice. The purpose of this note is to call attention on the fact that these trials do not seem to be extendable to man, in view of an agonism that one can predict for man, but not for mice, between topoisomerase 1 and a recently discovered angiogenesis inhibitor, angiostatin; leading one to anticipate in the majority of cases a worsening of angiogenesis in case of use of this drug on man. We thus recommend an immediate cease of these experiments.

As we have described in other papers (1), the scale resonance effects associated to protein biosynthesis allow one to predict, through the epigenetic regulation they exert on it, their metabolic agonisms and antagonisms from the data of their amino-acid sequence, by examining the corresponding quantum frequencies. Labeling 0 to 9 the ten distinct frequencies which remain associated to amino acids after they get fixed onto their transfer RNA, one observes a good dozen homologies between the 300 first amino acids of topoisomerase 1 and the sequence of angiostatin, an important inhibitor of angiogenesis:

Human DNA topoisomerase 1 (above in brackets: mouse)

52046464425451478444265654565485686556555485525624256542555

655555556540225565456548455585555381204154555554072233545453 \*\*\*\*\*

- (1) (4) (1) 544087333554453458384544348535545354355555854555540545535454

884053554235155313771554465833554785477549855534555444344253

47355258751535185552555545455545545580734544655841475453304 780804635505458845354444432541533233306595538644533943293544 502458454432284505549558531884553345484588549525555385813148 (3)

744541481045555053143303324835644463544055833574740542488845

333558375445475545535444748443044456454455043153783841243455 545543134544315442848148131443465813353755255445354415555414 188445215141535541535533525551358455545545351348554554140325 448443843319355903345548453585571914451454857 Human Angiostatin (homologies of successive quantum frequencies with topoisomerase 1 are underlined by identical typographic characters; above in brackets: mouse)

(1)

538425353040548803525354043355922323683872313632504554838434

(8) (5)

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443503938334355884834445355535632054840542535204535194252361 (6) (0) \*\*\*\*\*\* """" """"

608432573454455483843485483937334345895434438333333220338534

503054880431333206335692153363648335473354445483843405813936

334253895835432342233235541331335433335438604052880322333305

5352922533686553354834104354838434145039373343238958344553

This leads one to predict a strong metabolic agonism between those two proteins, and as a consequence that an inhibition of the former would reflect on the latter, thus des-inhibiting angiogenesis. On the contrary, most of these homologies (9 out of 12, among which the most significant ones underlined by +, \* et  $\sim$ ) disappear in the case of the mouse sequences (8 on angiostatin's side 2, 5 on topoisomerase 1 side, 4 on both sides together); from which follows that the results observed there cannot be extended to man.

This has particularly severe consequences when the other regulatory pathways of angiogenesis are themselves invalidated, the thrombomodulin way through a mutation of p53 and the platelet factor 4 way through a mutation of platelet-derived growth factor  $\beta$ ; which would necessitate at the very least a molecular oncogenic analysis before experimenting, so that we can only recommend an immediate cease of these experimentations under present circumstances.

In addition, coming after a similar observation concerning the object product leptin (3), this strengthens the necessity that the implications of homologies of successive frequencies associated to protein biosyntheses be taken into account before undertaking any study of this kind.

- (1) J. Sternheimer, Scaling waves, seminars given at the European University of Research (Paris), 1994-1995; Method for epigenetic regulation of protein synthesis by scale resonance, patent n° FR 92 06765 (1992). U. S. patent application n° SN 08/347.353; Application des homologies de suites de fréquences de la troponine C à la prédiction de son métabolisme, preprint (1995); Régulation épigénétique de la biosynthèse des protéines et prédiction de leur métabolisme à partir de leur séquence, preprint (1995).
- (2) M. S. D'Reilly et al., Angiostatin: a circulating endothelial inhibition that suppresses angiogenesis and tumor growth, Cold Spring Harbor Symp. LIX, p. 471 (1994); Cell 79, p. 315 (1994).
- (3) J. Sternheimer, Sur les différences métaboliques de la leptine (produit du gène ob) chez la souris et chez l'homme, preprint European University of Research (1995).